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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,271	02/06/2004	James M. Lipton	54275.8021.US01	8489

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EXAMINER	
TATE, CHRISTOPHER ROBIN	
ART UNIT	PAPER NUMBER
1655	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,271	LIPTON, JAMES M.	
	Examiner	Art Unit	
	Christopher R. Tate	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20, 22, and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 01 September 2006 is acknowledged and has been entered. Claims 1-20, 22, and 23 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions of nucleotide and/or amino acid sequences set forth in 37 CRR 1.821(a)(1) and (a)2. However (as amended) this application still fails to comply with the requirements of 37 CFR 1.821 through 1.825 - as set forth in the previous Office action. For example, SEQ ID NO: 5 is defined by claim 22 as being the 8-amino acid sequence VPKCCKPV (which translates into valine-proline-lysine-cysteine-cysteine-lysine-proline-valine). However the instant specification alternatively discloses SEQ ID NO:5 as defining His-DNle-Arg-Tryp-Phe-Lys-Pro-Val (see, e.g., paragraphs [0034] and [0043] of the instant specification), as well as VPK-Ac-CC-Ac- KPV (see, e.g., paragraph [0044] of the instant specification. It should also be noted that SEQ ID NO: 6 is also stated to be the sequence VPK-Ac-CC-Ac-KPV (see, e.g., paragraph [0035] of the instant specification). Further the CRF submitted 01 September 2006 defined SEQ ID NO:5 as being His-Xaa-Arg-Trp-Phn-Lys-Pro-Val. Accordingly, the specification gives alternative meanings as to the actual sequence defined by SEQ ID NO:5 (and the amendments to the specification presented within the 01 September 2006 response do not resolve this discrepancy concerning SEQ ID NO: 5). All sequences should be carefully reviewed to be sure they are in agreement throughout the specification as well as the CRF.

Claim Rejections - 35 USC § 112

Claims 19-20, 22, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 remains vague and indefinite by the ambiguous phrase "at least one derivative of *a*-MSH" - i.e., the metes and bounds of this phrase are not clearly nor adequately delineated. For example, a derivative of *a*-MSH could be anything from a carbon, hydrogen, or oxygen atom, an amino acid, a fragment of an amino acid, or some other inactive fragment of *a*-MSH (such as a short side-chain), to name a few.

In claim 22, the phrase "the derivative of *a*-MSH" lacks adequate antecedent basis. Please note that claim 22 ultimately depends from claim 19 which now recites "at least one derivative of *a*-MSH". Accordingly, it is suggested that claim 22 be amended to recited --the at least one derivative of *a*-MSH--.

All other cited claims depend directly or indirectly from claim 19 and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

With respect to claim 19, Applicants did not present arguments against the above USC 112, second paragraph rejection (and the amendments made to claim 19 presented within the 01 September 2006 response do not overcome the above rejection thereof).

Claim Rejections - 35 USC § 103

Claims 1-20, 22, and 23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Rajora et al. (Peptides, 1997 - IDS ref BB), Oktar et al. (Peptides, 2000 - IDS ref AY), and Lipton et al. (Annals NY Acad. Sci., 1998), in view of Ruepp (US

2002/0012708), Kennedy (internet article concerning J. Natural Health, 2002 - IDS ref AR), as well as the admitted state of the art - for the reasons set forth in the previous Office action which are restated below (please note that Applicant's traversal of what the Examiner considered to be Applicant's admission of the state of the prior art with respect to recent studies indicating the anti-inflammatory activity of alpha-MSH in the duodenal mucosa of celiac patients has been removed from the above USC 103 rejection, based upon Applicant's arguments presented within the 01 September 2006 response concerning this previous Examiner-alleged admission).

A pharmaceutical composition for treating malabsorptive conditions comprising alpha-MSH in combination with alpha-MSH derivatives and artichoke leaf extract is claimed, as well as a method of treating/preventing malabsorptive conditions of the gastrointestinal tract including colitis and other gastrointestinal inflammatory-type disorders via administering a therapeutically effective amount of alpha-MSH in combination with a therapeutically effective amount of artichoke extract to a subject having been diagnosed with such a disorder.

Rajora et al. beneficially disclose that alpha-MSH markedly improves inflammatory bowel disease characteristics, such as experienced in Crohn's disease and ulcerative colitis, in mouse models (see entire document including Abstract, Introduction, and Discussion).

Oktar et al. similarly beneficially disclose that alpha-MSH provides a broad and potent anti-inflammatory protective role on colonic lesions in rat models having induced colonic inflammation, such as experienced with Crohn's disease and inflammatory bowel disease (see entire document including Abstract, Introduction, Discussion).

Lipton et al. also beneficially disclose that alpha-MSH and derivatives thereof provides effective anti-inflammatory activity versus all major models of inflammation including experimental inflammatory bowel disease (see, e.g., Abstract). None of the first three cited references expressly teach the further incorporation and/or administration of artichoke leaf extract to such a subject.

Ruepp beneficially teaches that artichoke leaf extract is useful as an active agent in treating inflammatory diseases of the bowel, including Crohn's disease (see, e.g., paragraphs [0150], [0155], and claim 1).

Kennedy also beneficially discloses that artichoke leaf extract provided improvement to patients with irritable bowel syndrome, a well known inflammatory bowel disease (see first page of internet article: IDS ref AR - concerning the teachings of the 1992 Kennedy publication). In addition, please note that Applicant readily admits that artichoke leaf extract has been shown in the art to reduce symptoms of irritable bowel syndrome (see, e.g., paragraph [0015]).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the instant ingredients for their known benefit (i.e., treating an inflammatory bowel disease/disorder such as from among those instantly claimed) - as well as to treat a subject having been diagnosed with such an inflammatory bowel disease/disorder - since each ingredient is well known in the art for the same purpose, based upon the beneficial teachings provided by the cited references as a whole with respect to their demonstrated gastrointestinal anti-inflammatory activity (as discussed above), and for the following reasons.

It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Sussman, 1943 C.D. 518; In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960) - also see In re Kerkhoven, 626 F.2d 846, 850, 205 U.S.P.Q. 1069 (CCPA 1980). This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients. Applicants invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g., synergism) is therefore *ipso facto* unpatentable. The adjustment of particular conventional working conditions (e.g., treating a particular type of inflammatory gastrointestinal disease/disorder, and/or determining therapeutically effective amounts of such ingredients therein) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references (as well as from the admitted state of the art), it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references (as well as the admitted state of the art), especially in the absence of evidence to the contrary.

Applicants' arguments concerning the above USC 103 rejection have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicant argues that the Rajora et al investigated the effects of alpha-MSH in experimental inflammatory bowel disease in the mouse model but that the mouse model system does not teach anything about alpha-MSH to malabsorption diseases, *per se*. Applicant further argues that Oktar et al. used rat models to mimick inflammatory bowel disease, and similarly, that Lipton et al. discuss mounting evidence (but not conclusive evidence) that alpha-MSH inhibits inflammatory reactions in animal models of inflammatory, and also that Lipton et al. do not speak specifically to malabsorption diseases. However, with respect to Applicant's arguments concerning the references not teaching the treatment of malabsorption diseases, it is clear from the teachings provided by the cited references (as a whole) that the claimed ingredients were well known at the time to each be useful in treating various types of inflammatory bowel diseases including, e.g., Crohn's and/or ulcerative colitis - which, as instantly disclosed and claimed (and as well known in the art) read upon malabsorption diseases/conditions of the intestinal tract (see, e.g., paragraph [0007] of the instant specification and instant claim 2).

Further, Applicant has argued and discussed references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which make up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the references.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

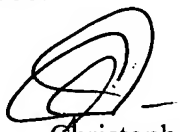
Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Tate whose telephone number is (571) 272-0970. The examiner can normally be reached on Mon-Thur, 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Christopher R. Tate
Primary Examiner
Art Unit 1655